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EXAMINER
CHEN, LIPING

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/17/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/714,790	Applicant(s) SCHMIDT-ULLRICH ET AL.	
	Examiner Liping Chen	Art Unit 1632	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Liping Chen of Group Art Unit 1632.

Restriction/Election

Applicant's election without traverse of Group III, claims 19-32, in Paper No. 8, is acknowledged. Claim 1-18 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claims 1-32 are pending and claims 19-33 are under current consideration.

Priority

Priority claimed to provisional application 60/165,940 filed 11/17/1999.

Specification

The disclosure is objected to because of the following informalities:

The drawings are objected in view of the reasons set forth in the attached PTO-948. A complete response to this office action must include a response to the objection or a filing of corrected drawings so as to obviate the objection.

Description of the Drawings for Fig. 13 is objected to because it states "Transduction efficiency of Ad-EGFR-CD533 at increasing MOI. However, the Fig. 13 is a result of transduction efficiencies of MDA cells with Ad-LacZ at different MOI.

Fig. 20 B is further objected to because the labels "in vivo" and "in vitro" are between both lanes. It is not clear which lane is for the result of in vivo, which lane is for the result of in vitro.

Page 50, line 27, states "after repeated radiation exposures (Figure 31)". It is suggested this be rewritten to state "after repeated radiation exposures (Figure 33)".

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 19 is directed to a method for radiosensitizing cancer cells, comprising delivery to cancer cells an effective dose of an expressible nucleic acid molecule encoding a mutant epidermal growth factor receptor (EGFR); claims 20-32 are further directed to different embodiments: claim 20 is directed to the mutant EFFR of claim19 is EGFR-CD533, Claims 21-24 are directed to the expressible nucleic acid molecule of claim 19 is a DNA molecule (claim 21), is in an expression cassette (claim 22), is Ad-EGFR-CD533 (claim 23), and is an RNA molecule (claim 24), respectively; claims 25-29 are directed to the step of delivering of claim 19 is accomplished by administration to a patient in need by oral delivery (claim 26), systemic delivery (claim 27), delivery *in situ* at the cancer locus (claim 28), or carried out via viral vector, liposome or direct injection of nucleic acid (claim29); claims 30-32 are directed to the cancer cells of claim 19 are mammary cancer cells (claim 30), glioma cells (claim 31), or cancer cells expressing EGFR (claim32).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, while a written description for mutant form of EGFR, such as EGFR-

CD533 and EGFR missing more or less carboxy terminal region comparing with EGFR-CD533 (specification, page 15, line 9 to page 17, line 27) is generally understood, there is no written description regarding different mutants other than a deletion of carboxy terminal region of EGFR that are dominant-negative mutants and can be used for radiosensitizing cancer cells. The specification states different types of mutants, such as mutants that are missing portions of other regions of the protein, or resulting from various point mutations, substitutions, frame shift mutations, and insertions are included in the instant invention (specification, page 16, line 14 to page 17, line 2). However, there is no written description regarding the detailed chemical structure of each type of mutant that is a dominant-negative mutant and possesses the required function for radiosensitizing cancer cells. Therefore, with the exception of the EGFR with a carboxy terminal truncated, such as EGFR-CD533, the skilled artisan cannot envision the detailed chemical structure of any other mutants that are dominant-negative mutants and can be used for radiosensitizing cancer cells. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a

whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In the instant case, only EGFR with carboxy terminal truncated, such as EGFR-CD533, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 19-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling directly delivering to ~~a~~ cancer cells an effective dose of an expressible nucleic acid molecule encoding a carboxy terminal truncated EGFR for inhibiting the radiation-induced proliferation of cancer cells, does not reasonably provide enablement for delivering to a cancer cells an effective dose by the routes other than directly injection, nor enablement for radiosensitizing cancer cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 19 is directed to a method for radiosensitizing cancer cells, comprising delivery to cancer cells an effective dose of an expressible nucleic acid molecule encoding a mutant epidermal growth factor receptor (EGFR); claims 20-32 are further directed to different embodiments: claim 20 is directed to the mutant EFFR of claim19 is EGFR-CD533, Claims 21-24 are directed to the expressible nucleic acid molecule of claim 19 is a DNA molecule (claim 21), is in an expression cassette (claim 22), is Ad-EGFR-CD533 (claim 23), and is an RNA molecule (claim 24), respectively; claims 25-29 are directed to the step of delivering of claim 19 is accomplished by administration to a patient in need by oral delivery (claim 26), systemic delivery (claim 27), delivery *in situ* at the cancer locus (claim 28), or carried out via viral vector, liposome or direct injection of nucleic acid (claim29); claims 30-32 are directed to the cancer cells of claim 19 are mammary cancer cells (claim 30), glioma cells (claim 31), or cancer cells expressing EGFR (claim32). The specification provides detailed working examples to elucidate the mechanisms related with EGFR mediated cell proliferation during radiation therapy using mammary carcinoma cell lines, MCF-7 and MDA-MB-231 containing doxycycline (Dox)-inducible EGFR-CD533, a EGFR lacking the C-terminal 533 amino acids (see specification, page 22, line 1 to page 36, line 20, and Fig. 1-12). The specification also provides working examples for *in vitro* delivery of Ad-EGFR-CD533 into MDA cells (specification, page 40, line 26 to page 41, line 2, and Fig. 14) and *in vivo* Ad-EGFR-CD533 infusion (see specification, page 39. line 7-19 and Fig. 21) into MDA

tumor xenografts produced by subcutaneous inoculation of tumor cells into the right hind leg of 4-6 week old athymic female NCr-nu/nu mice (specification, page 37, line 3-11), resulted in an increased rediosensitization of MDA cells associated with EGFR-CD533 expression *in vitro* (specification, page 41, line 19 to page 42, line 6, and Fig. 17) and in vivo (specification, page 43, line 10 to page 44, line 7, and Fig. 23). Similarly, the specification provides working examples for decreased surviving fraction of U-87 MG, a human glioblastoma cell line, and U-373 MG, originally isolated from a human anaplastic astrocytome, transduced with Ad-EGFR-CD533 after exposure to radiation (specification, page 44, line 12 to 18, page, 49, line 16 to page 50, line 18, and Fig. 30-32), and examples of decreased survival rate of U-87 MG tumor xenografts (specification, page 50, line 19 to page 51, line 2, and Fig. 33), produced by subcutaneous inoculation of tumor cells into the right hind leg of 2 to 3 month old athymic female NCr-nu/nu mice (specification, page 45, line 6-15), after exposure to radiation. These data do not suggest that decreased tumor survival rate is resulted from a direct radiosensitization of cancer cells. There is no evidence that decrease tumor survival rate is a result of increased killing of tumor cells by radiation. Moreover, the specification does not provide any teaching or guidance as how to delivery effective amount of Ad-EGFR-CD533 or EGFR-CD533 by any other delivery vectors, such as retroviral vector or liposome to any tumors by the route of other than direct infusion to reach an effective amount EGFR-CD533 expression in the target site. With regard to gene delivery in gene therapy, Verma et al. (Nature,

389:239-242, 1997) points out that the problems are the lack of efficient delivery systems, lack of sustained expression and host immune reactions (Verma, page 239, col. 1). Rozenberg et al. (S.T.P. Pharma Sciences 11:21-30, 2001) state that requirements for a vector to have successful gene delivery include ability to produce high titer vector particles, ability for efficient transgene expression for the desired duration, and low immunogenicity of the vector (Rozenberg, page 21, left col. sec. parag.). Although using non-viral vector such as liposome can limit immunologic reactions and mutations caused by viral delivery system, the limited efficacy and short duration of transgene expression has been recognized in the art since the time of filing (Nishikawa et al. Human Gene therapy 12:867-870, 2001). Nishikawa et al. (2001) explain that nonviral vectors, such as naked DNA and cationic lipid (liposome) or polymer, encounter many hurdles that result in diminished gene transfer in target cells (Nishikawa, Abstract). Nishikawa further explain that the physicochemical properties of a DNA-vector complex will affect its passage through capillaried, extravasation, capture by the mononuclear phagocytes, and uptake by target cells when using nonviral vectors. Interaction with blood components would alter these biodistribution. Since the complex is routed mainly to endosomes/lysosomes after its cellular uptake, it should be released into the cytoplasm and delivered to the nucleus (Nishikawa, page 862, col. 1 first full parag.). Further, Balicki (Medicine 81:69-86, 2002) compares several vectors, such as Retrovirus, Adenovirus, Adeno-Associated Virus, Herpes Simplex Virus in

different generation as well as liposome, protein/peptide and naked DNA, by means of cell target, chromosomal integration and immunogenicity (Balicki, page 70, Table 1) and teaches that the most common and useful strategy is to deliver the gene of interest to the nucleus and points out the extracellular barriers for such delivery include degradative enzymes (Balicki, page 70, left col. first parag.). Taken together, the art teaches the fate of gene delivery is determined by vector used, gene encoded, protein produced, and cells targeted, these factors influence the fate of a transgene dramatically. Although the specification provides detailed teaching for directly infusion Ad-EGFR-CD533 into MDA tumor exenografts and U-87 MG tumor xenografts, the specification failed to provide evidence or teaching as to use different vectors, such as different viral vectors, liposomes, and naked nucleic acid for EGFR-CD533 delivery by delivery routes other than direct infusion, such as systemic delivery (pertaining to instant claim 27) and oral delivery (pertaining to instant claim 26), delivery the Ad-EGFR-CD533 to glioma cells *in vivo* (pertaining to instant claim 31). Furthermore, the animal used in the instant invention is athymic female NCr-nu/nu mice. With regard to nude mice model, the art teaches that the growth of human tumors in immunocompromised mice does not reflect the natural and physiological growth and spread of tumors in non-immunocompromised animals (Gura, Science 278:1041-1042, 1997). Gura explains that for this reason, ".. drugs tested in the xenografts appeared effective but worked poorly in humans. " (Gura, page 1041, col. 2, parag. 3).

Therefore, in view of the results obtained from the working examples based on nude mice model, the lack of evidence that the decreased tumor survival rate is the result of radiosensitized cancer cells, the lack of evidence or teaching as how to deliver an effective amount of expressible nucleic acid molecule encoding a mutant EGFR into any cancer cell in vivo other than direct delivery, based upon the nature of the invention, the state of the prior art, the unpredictability in gene delivery in gene therapy, lack of teaching as any mutant EGFR except of EGFR-CD533 and other C-terminal truncated EGFR will result the same effect as using EGFR-CD533, the claimed invention would have required one skilled in the art to engage in an undue amount of experimentation without a predictable degree of success to achieve any specific and the breath of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 19-23, 25, 29 and 32 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Contessa et al. (Clinical Cancer Res. 5:405-11, 1999).

Claim 19 is directed to a method for radiosensitizing cancer cells, comprising delivery to cancer cells an effective dose of an expressible nucleic acid molecule

encoding a mutant epidermal growth factor receptor (EGFR); claim 20 is directed to the mutant EFFR of claim19 is EGFR-CD533, Claims 21-23 are directed to the expressible nucleic acid molecule of claim 19 is a DNA molecule (claim 21), is in an expression cassette (claim 22), is Ad-EGFR-CD533 (claim 23); claims 25 and 29 are directed to the step of delivering of claim 19 is accomplished by administration to a patient in need (claim 25) or carried out via viral vector (claim 29); and claim 32 is directed to the cancer cells of claim 19 express EGFR.

Contessa et al. teach methods of construction of MCF-TR5-EGFR-CD533 and MDA-TR15-EGFR-CD533 cell lines using parental MCF-7 and MDA-MB231 cell lines (Contessa, page 406, left col. first full parag.), which contain EGFR-CD533 that is inducibly expressed by Dox treatment (Contessa, Abstract, page 406, right col. sec full parag., and Fig. 1), where both parental cell line express EGFR (Contessa, page 407, right col. top parag., page 409, left col. first full parag. and Fig. 4). Further, Contessa et al. suggest the EGFR-CD533 can be used for therapeutic application through efficient transient transduction of carcinoma cells using adenovirus EGFR-CD533. Thus, Contessa et al. clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19-25 and 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greene et al. (U.S. Patent No. 6,417,168, issued 07/09/2002, filed 07/08/1998) in view of Contessa et al. (Clinical Cancer Res. 5:405-11, 1999).

Claim 19 is directed to a method for radiosensitizing cancer cells, comprising delivery to cancer cells an effective dose of an expressible nucleic acid molecule encoding a mutant epidermal growth factor receptor (EGFR); claims 20-32 are further directed to different embodiments: claim 20 is directed to the mutant EFFR of claim19 is EGFR-CD533, Claims 21-24 are directed to the expressible nucleic acid molecule of claim 19 is a DNA molecule (claim 21), is in an expression cassette (claim 22), is Ad-EGFR-CD533 (claim 23), and is an RNA molecule (claim 24), respectively; claims 25, 27-29 are directed to the step of delivering of claim 19 is accomplished by administration to a patient in need (claim 25) by systemic delivery (claim 27), delivery *in situ* at the cancer locus (claim 28), or carried out via viral vector, liposome or direct injection of nucleic acid (claim29); claims 30-32 are directed to the cancer cells of claim 19 are mammary cancer cells (claim 30), glioma cells (claim 31), or cancer cells expressing EGFR (claim 32).

Claim 19 recites an intended use of an expressible nucleic acid encoding a mutant EGFR. It is noted that an intended use of the compound does not constitute

a step in the method as claimed. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure or composition, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. In re Hirao , 535 F.2d 67, 190 USPQ 15 (CCPA 1976); Kropa v. Robie , 88 USPQ 478, 481 (CCPA 1951).

Greene et al. ('168) teach methods of treating individuals who have erbB protein mediated tumors comprising the steps of administering to such individuals nucleic acid molecules that encode a protein that dimerizes with said erbB protein, such as erbB1 (EGFR) and erbB2 (p185), and that is deficient in tyrosine kinase activity, and exposing said individual to a therapeutically effective amount of anti-cancer radiation ('168, col. 5, line 38-46, col. 4, line 10-30, and col. 15, line 41-53), where the tumor cells include the tumors that comprise an EGFR species such as wild type or mutant EGFR ('168, col. 6, line 8-16, pertaining to instant claim 32), malignant human gliomas ('168, col. 11, line 50-61, and col. 19, line13-15, pertaining to instant claim 31) or human mammary cell line HC11 cells ('168, col. 34, line 60-63, pertaining to instant claim 30). Greene et al. ('168) further teach the nucleic acid molecules can be delivered in DNA form by viral vector delivery in an expression cassette ('168, col. 16, line 42-56, and col. 28, lines 10-32, pertaining to instant claims 21-22 and 29) or liposome mediated transfer ('168, col. 17, line 4-22, pertaining to instant claim 29); or in RNA form by retrovirus delivery ('168, col. 16,

line 57-63, pertaining to instant claim 24), and suggest the delivery routes such as intratumor, intravenous and subcutaneous administration ('168, col. 17, line 38-44). Further more, Greene et al. ('168) teach an example of a nucleic acid sequence encodes truncation species of rat p185 comprising either N-terminal or C-terminal deletions which dimerizes with either human p185 or human EGFR and which lacks tyrosine kinase activity ('168, col. 21, line 6-21) can be used for the treatment. Greene et al. does not explicitly teach to use a nucleic acid encoding C-terminal deletions of EGFR for the treatment.

Contessa et al. teach MCF-TR5-EGFR-CD533 and MDA-TR15-EGFR-CD533 cells containing EGFR-CD533 that is inducibly expressed by Dox treatment (Contessa, Abstract, page 406, right col. sec full parag., and Fig. 1). Contessa et al. further demonstrate that in the presence of Dox, radiation activated EGFR-WT Tyr phosphorylation is inhibited by EGFR-CD533 expression (Contessa, page 407, right col. top parag., page 409, left col. first full parag. and Fig. 4) and associated inhibition of MDA-TR15-EGFR-CD533 cell growth after radiation (Fig. 6) . Contessa et al. cure the deficiency of Greene et al. ('168) in that it provides an EGFR mutant EGFR-CD533 that behaves as a dominant-negative mutant and inhibits tumor cell growth after radiation.

One of skill in the art of tumor gene therapy would be motivated to use EGFR-CD533 as a C-terminal deletion of EGFR instead as an alternate choice for the treatment taught by Greene et al. ('168) with a reasonable expectation of

success. Because EGFR-CD533 meets the requirement of Greene et al, that is a nucleic acid molecules that encode a protein that dimerizes with said erbB protein, such as erbB1 (EGFR) and erbB2 (p185), and that is deficient in tyrosine kinase activity. Therefore, at the time the invention was made it would have been prima facie obvious to modify the teaching of Greene et al. to used a nucleic acid encoding EGFR-CD533 for the treatment taught by Greene et al. ('168).

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liping Chen, whose telephone number is (703) 305-4842. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time). Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Dianiece Jacobs, Patent Analyst, at (703) 305-3550. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center

located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-8724.

Liping Chen, Ph.D.
Patent Examiner
Group 1632

DAVE T. NGUYEN
PRIMARY EXAMINER